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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,478	07/29/2002	Kevin Jeffrey Barnham	16153	8704

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EXAMINER

KOSAR, ANDREW D

ART UNIT	PAPER NUMBER
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1654

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/031,478

Applicant(s)

BARNHAM ET AL.

Examiner

Andrew D. Kosar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41 and 43-46 is/are pending in the application.
- 4a) Of the above claim(s) 1-30, 37, 43 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-36, 38-41, 44 and 45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Response to Arguments/Amendments

Applicant's arguments and amendments filed October 26, 2006 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant has introduced new claims 45 and 46 and cancelled claim 42. Claim 45 has been included in the elected invention and have been examined on the merits, as *in vivo* metal ions are inherently present. Claim 46 does not read upon the examiner's species (nicotine) and has not been included.

Claims 1-30, 37, 43 and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 10, 2006.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-36, 38 and 39 remain rejected under 35 U.S.C. 102(b) as being anticipated by SHAO for the reasons of record and those set forth below.

The instant claims are drawn to inhibiting binding of metal ions or preventing A β aggregation (amyloidosis).

Applicant argues that "it is believed that nicotine does not inhibit the interaction of A β with metal ions" and provides further arguments that assert it is, "unlikely that nicotine would recognize all structural forms of A β to effectively inhibit the interactions of A β with metal ions"

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(Remarks, page 10). Applicant further asserts that the binding experiment of Shao could not establish the ability to inhibit A β metal binding.

Respectfully, MPEP § 2145 states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). Here, Applicant has provided no evidence to rebut the rejection set forth.

Additionally, the examiner disagrees with Applicant's arguments. Shao clearly teaches inhibition of amyloidosis, and states as much (below). Binding to His13 and His14 blocks metal binding, as absent an free valence- specifically the valence being used in the binding of nicotine- it is chemically impossible for any metal to bind. Analogously, it is akin to parking your car at the grocery store. If there is a car in the space you want, you cannot park there, and are effectively inhibited from parking there.

Furthermore, though not relied upon in the rejection, in rebuttal to Applicant's arguments that the methodology of Shao is flawed because Salomon could not establish the inhibition of A β , Salomon is cited by Hellström-Lindhahl (E. Hellström-Lindhahl *et al.* Br. J. Neurosci. (2004) 19, pages 2307-2310) as teaching, "A direct effect of nicotine has been observed *in vitro*, with the alkaloid both preventing and breaking down amyloid fibrils" (page 2708). Respectfully, the art recognizes the *in vitro* effect.

Shao teaches that, "As for the nicotine-inhibition to β -amyloidosis, the NMR work established that nicotine binds to the His13 and His14 side-chains of the Tyr10-Val24 α -helix,

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and this prevented an α -helix \rightarrow β -sheet conversion and β -amyloid precipitation.” [*citation removed by Examiner*] (page 767).

Thus, in conducting the NMR, one is inherently practicing the method, as binding of nicotine to β -amyloid protein at His13 and His14 inherently ‘blocks’ the N-terminus in such a way that binding of metal ions at said His residue(s) is/are inhibited.

Furthermore, because nicotine meets the requisite structural characteristics of claim 31, it necessarily must possess the same function, e.g. binding to specific sites on the A β protein, specific inhibition of various cations, etc. Additionally, because nicotine binds to A β it necessarily must ‘comprise’ a targeting moiety.

Claims 31-36, 38-41, 44 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by BRENNER (D.E. Brenner *et al.* Neurology (1993) 43, pages 293-300) as evidenced by Shao, *supra*.

The instant claims and teachings of Shao are presented *supra* and are generally drawn to treating AD in a patient.

Brenner teaches subcutaneous injection of nicotine to AD patients, “improved attention and information processing” (page 298), meeting the limitations of ‘treating a patient with AD’ and subcutaneous injection of nicotine to a human necessarily requires a pharmaceutically acceptable carrier. As stated *supra*, nicotine is known to bind A β and thus inhibits metal binding. The human body inherently has circulating metal ions that are capable of binding the His residues of A β .

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Conclusion

Applicant's elected species remains free of the prior art for the reasons of record.

The prior art made of record on the enclosed PTO- 892 and not relied upon is considered pertinent to applicant's disclosure.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 1-30, 37, 43 and 46 drawn to an invention nonelected with traverse in the response filed January 10, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913.

The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


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Patent Examiner
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